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Determinants for the adoption of angiotensin II receptor blockers by general practitioners

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Abstract

Results of studies conducted 10–20 years ago show the prominence of commercial information sources in the adoption process of new drugs. Over the past decade, there has been a growing emphasis on practicing evidence-based medicine in drug prescribing. This raises the question whether professional information sources currently counterbalance the influence of commercial information sources in the adoption process. The aim of this study was to identify determinants influencing the adoption of a new drug class, the angiotensin II receptor blockers (ARBs), by general practitioners (GPs) in The Netherlands. A retrospective study was conducted to assess prevalent ARB prescribing for hypertensive patients using the Integrated Primary Care Information (IPCI) database. We conducted a survey among all GPs who participated in the IPCI project in 2003 to assess their exposure to commercial and professional information sources, perceived benefits and risks of ARBs, perceived influences of the professional network, and general characteristics. Multilevel logistic regression was applied to identify determinants of ARB adoption while adjusting for patient characteristics. Data were obtained from 70 GPs and 9470 treated hypertensive patients. A total of 1093 patients received ARBs (12%). GPs who reported frequent use of commercial information sources were more likely to prescribe ARBs routinely in preference to other antihypertensives, whereas GPs who used a prescribing decision support system and those who were involved in pharmacotherapy education were less likely to prescribe ARBs. Other factors that were associated with higher levels of ARB adoption included a more positive perception of ARBs regarding their effectiveness in lowering blood pressure, and working in single-handed practices or in rural areas. Aside from determinants related to the patient population, adoption of a new drug class among Dutch GPs is still determined more by their reliance on promotional information than by their use of professional information sources.

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Introduction

There is a lively debate about which medication to choose in hypertensive treatment, fuelled by controversy about possible limitations of large

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randomized clinical trials and interpretation of their findings as well as by financial interests and concerns (Frohlich, 2003; Moser, 2003). Quality improvement programmes stress the relevance of implementing clinical guidelines and practicing evidence-based medicine, governments aim for cost containments, and pharmaceutical industries aim to make more profits (Lexchin, 2002). Amidst these forces, physicians have to decide about the place of new antihypertensive drugs. Results of studies that were conducted more than 20 years ago showed the prominence of commercial information sources in the adoption process of new drugs and the minor influence of professional information sources (Avorn, Chen, & Hartley, 1982; Peay & Peay, 1984). The influence of commercial information is still a matter of concern, but there are few recent empirical studies on the impact of various information sources on drug choice and prescribing behaviour (Caamano, Figueiras, & Gestal-Otero, 2002; Wazana, 2000). In an environment with a growing emphasis on evidence-based medicine, professional information sources might counterbalance the influence of commercial information sources in the adoption process.

Angiotensin II receptor blockers (ARBs) were introduced in the market in 1995 as a new drug class for hypertension after proving efficacy in lowering blood pressure. Evidence on hard endpoints such as cardiovascular morbidity and mortality in patients with hypertension was not available until 2002 (Dahlof et al., 2002). Due to this lack of evidence on hard endpoints, the high costs, and the availability of alternatives with proven effectiveness, ARBs have not been recommended as first-line treatment for essential hypertension in most treatment guidelines (Grobbee, Tuut, & Hoes, 2001; JNC, 1997). Nevertheless, the use of ARBs has increased remarkably in the last 10 years (Garcia del Pozo, Ramos Sevillano, de Abajo, & Mateos Campos, 2004; Greving et al., 2004).

Adoption rates of new drugs vary among physicians and by type of drug (Dybdahl, Andersen, Sondergaard, Kragstrup, & Kristiansen, 2004; Inman & Pearce, 1993; McGavock, Webb, Johnston, & Milligan, 1993; Steffensen, Sorensen, & Olesen, 1999; Tamblyn, McLeod, Hanley, Girard, & Hurley, 2003). The adoption of new treatments in clinical practice is the result of many factors. Based on Rogers' theoretical model for the diffusion of innovations, the following factors can be identified: (1) information sources used, (2) perceived char-

acteristics of the new drug, (3) professional network and norms, (4) general physician characteristics (Rogers, 1995). In addition to this general framework, decision-making theories can help us understand how treatment choices are made on an individual level (Sox, Blatt, Higgins, & Marton, 1988). Differences in drug choice can be related to different perceived characteristics or expectations about drugs, but also to differences in the relative importance or value assigned to the various drug aspects (Denig, Haaijer-Ruskamp, & Zijssling, 1988; Denig, Witteman, & Schouten, 2002; Segal & Hepler, 1985).

Physicians who frequently prescribe new drugs have shown to be less cost-consciousness in prescribing and to rely more on commercial information sources (Jacoby, Smith & Eccles, 2003; Prosser & Walley, 2003). Adoption of new drugs was also found to be associated with physician gender, specialty, medical school, years since graduation, practice location, practice size, and proportion of elderly in the practice (Steffensen et al., 1999; Tamblyn et al., 2003). On the other hand, characteristics of the patient population of a physician may also determine the need for prescribing new treatments (Bourgault, Rainville, & Suissa, 2001; Florentinus et al., 2005; Klungel, de Boer, Paes, Seidell, & Bakker, 1998). To date, none of the studies looking at determinants of drug adoption considered the influence of all factors simultaneously and took possible differences in patient populations into account.

The aim of this study was to identify determinants for adoption of ARBs in routine prescribing for hypertension by linking physician related characteristics to their actual prescribing behaviour while adjusting for patient characteristics.

Methods

Setting

The data reported in this study were collected from 75 general practitioners (GPs) contributing to the Integrated Primary Care Information (IPCI) database in 2000–2003. The IPCI database is a general practice research database which contains information from computer-based patient records of GPs in The Netherlands and is maintained by the Erasmus Medical Center (van der Lei et al., 1993). The first practice was enrolled in the IPCI project in 1992 but a large proportion of practices started to

contribute from 1998 onwards. In The Netherlands, GP records contain all relevant medical information on individual patients, since patients are registered to a single GP who has a gatekeeper role. To maximize completeness of the data, GPs who participate in the IPCI project are not allowed to use paper-based records. The computer-based records contain information on patient demographics, symptoms (free text), diagnosis (using the International classification for primary care), referrals, laboratory measurements, and drug prescriptions (coded according to the anatomic therapeutic chemical (ATC) classification system)(WHO Collaboration Centre for Drug Statistics Methodology, 1999; World Organization of Family Doctors (WONCA), 1998). The database complies with European Union guidelines on the use of medical data for medical research, and has been proven valid using different reference methods for pharmaco-epidemiological research (Greving et al., 2004; Vlug et al., 1999). The Scientific and Ethical Advisory Group of the IPCI project approved the study.

Physician survey data

The GPs were asked to complete a questionnaire, designed to be short and easy to complete in order to optimize the response rate (Edwards et al., 2002). Major domains of the questionnaire included factors that may influence drug choice and the adoption of new drugs (Denig et al., 1988; Rogers, 1995), i.e.: use of information sources, perceived benefits and risks of the drugs, the importance attached to specific drug characteristics, professional network, and general physician characteristics. The questionnaire items and format were pilot tested for clarity and face validity among eight GPs not related to the study population and revised accordingly. A copy of the questionnaire can be requested from the corresponding author.

GPs could first indicate how often they used various information sources in general (scientific medical journals, practice guidelines, national drug compendium, conferences/continuing education, formularies, computerized prescribing support system, pharmacotherapy counselling groups). Next, they were asked how often they would use various sources for information on the treatment of hypertension on a scale from 1 (never) to 6 (always). Included were four professional sources (i.e. scientific medical journals, practice guidelines, national

drug compendium, conferences/continuing education) and four commercial sources (i.e. pharmaceutical representatives, journal advertisements, direct mailings, sponsored meetings). Secondly, expectancies and values regarding different antihypertensive drug treatment aspects were measured. GPs were asked to grade their expectations regarding efficacy, user-friendliness of the dosage schedule, side effects and costs for each antihypertensive drug class on a scale from 1 (low on efficacy and user-friendliness; high on side effects and costs) to 10 (high on efficacy and user-friendliness; low on side effects and costs). This was used to calculate the perceived relative expectancy of ARBs in comparison to the average perceived expectancy of other antihypertensive drug classes (i.e. diuretics, beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors (ACE-inhibitors)). GPs were also asked to rate the importance of values attached to these aspects for their choice of antihypertensive treatment on a scale from 1 (not important) to 6 (important). Thirdly, GPs could indicate how often they perceived the influence of colleagues, hospital physicians and patients to prescribe new antihypertensive drugs on a scale from 1 (never) to 6 (always). Finally, GPs provided data on demographic details including age, gender, practice type (single-handed versus partnership), practice location (urban versus rural), practice size, workload, and work experience. GPs were also asked about their membership in professional societies, their involvement in developing guidelines, and their involvement in providing pharmacotherapy education. Most Dutch GPs participate in pharmacotherapy counselling groups that meet at least four times a year to exchange information and discuss pharmacotherapy. Not all GPs, however, are personally involved in preparing the content of these meetings. Additionally, GPs were asked about their participation in trials with antihypertensive drugs in the past five years.

The initial survey mailing was made in May 2003. Telephone reminders and one follow-up mailing were made to non-respondents to encourage a high response rate.

Prescribing data for measuring adoption of ARBs

We were interested in the adoption of ARBs in routine prescribing. Therefore, we looked at prevalent prescribing of ARBs to patients with hypertension in the year 2000 as indicator for adoption. This includes prescribing as initial or

follow-up treatment, both monotherapy and combination therapy. To assess prevalent prescribing, we retrieved all prescriptions for antihypertensive drugs (diuretics, beta-blockers, calcium channel blockers, ACE-inhibitors, and ARBs) for patients with hypertension in a 6-months period before our index date (the first Wednesday in October 2000). This was roughly five years after the introduction of the first ARB in the Dutch market, and two years before the results of large clinical trials on cardiovascular endpoints on ARBs became available. Details on identification of these patients have been published elsewhere (Greving et al., 2004). In brief, hypertension was identified from the medical records by a search on ICPC-code (K85, K86, and K87) and free text search on the diagnosis hypertension followed by manual review. Data were also collected on presence of comorbidities and referrals to an internist or cardiologist.

Statistical analysis

Multivariable analyses were conducted to assess the influence of physician level determinants on prescribing ARBs rather than other antihypertensive drugs. These analyses were preceded by univariable analyses and data reduction procedures to reduce the number of independent variables. We assessed whether the use of professional and commercial information sources on hypertension treatment could be summated in two multi-item scales with acceptable reliability (Cronbach's alpha > 0.70).

Determinants of adoption were studied by linking physician related characteristics and views to their actual prescribing behaviour of ARBs, taking into account the possible effect of patient characteristics. Because of the hierarchy in the data, i.e. clustering of patients that receive care from the same GP, we used multilevel logistic regression with patient characteristics included at the first level and GP characteristics at the second level. All analyses were performed with MLwiN software, version 1.2. The multivariable multilevel models were built in two steps. First, we developed a multivariable model for all physician related variables, entering all variables that were significant at $p < 0.10$ level in the univariable analysis. All variables that remained significant at $p < 0.05$ level maintained into the final model (model 1). Second, we investigated the influence of physician related characteristics after adjustment for patient characteristics that could affect the prob-

ability of receiving ARBs, such as age, gender, presence of comorbidities, and referrals (model 2) (Garcia del Pozo et al., 2004; Greving et al., 2004). The influence of the variables on prescribing of ARBs is presented as odds ratios (OR) with 95% confidence intervals (CI).

Results

Study population

Seventy-two GPs completed the questionnaires (response rate: 96%). Two GPs who worked in partnership practices were excluded since they had less than 20 registered hypertensive patients. The final study population comprised 70 GPs and 9470 patients with hypertension who had received anti-hypertensive medication in the year 2000. These 70 GPs had a mean age of 49 years (SD 6), and were mainly male (84%). The majority worked full-time (65%), mostly in partnership practices and in urban areas. The mean size of practice was 2435 patients (SD 534). In this study, the percentage of males was slightly higher, the percentage of GPs working in urban areas was higher, and GPs were significantly older compared with the entire population of Dutch GPs. There were no substantial differences in terms of practice type and workload.

Of the 9470 patients treated for hypertension, 1093 patients were being prescribed ARBs (12%). There was a considerable variation in the use of ARBs between GPs (interquartile range, 6–15%). Thirty-two percent of the patients were treated with ACE-inhibitors, 21% received calcium channel blockers, 41% beta-blockers, and 41% received diuretics. On average, patients received 1.5 anti-hypertensive drug prescriptions. Patients who were treated with ARBs were more likely than other hypertensive patients to be younger, to have asthma or chronic obstructive pulmonary disease, and were more likely to have been referred to an internist or cardiologist (Table 1).

Multi-item scales

The four-item scale on use of commercial information sources showed a high internal consistency (Cronbach's alpha = 0.77), and a summated score was therefore used for these commercial information sources. No multi-item scale could be identified for professional information sources because of lack of internal consistency (Cronbach's alpha < 0.7).

Table 1
Characteristics of prevalent users of angiotensin II receptor blockers versus other antihypertensive drugs classes in 2000

Characteristics	Angiotensin II receptor blocker users (<i>n</i> = 1093)	Users of other antihypertensive drug classes (<i>n</i> = 8377)	<i>P</i> value
	Mean ± SD or number (%)		
Age (years)	64.2 ± 12.6	66.0 ± 12.9	<0.001
Female	670 (61)	5189 (62)	0.691
Number of additional comorbidities	1.2 ± 1.3	1.2 ± 1.3	0.112
Angina pectoris	141 (13)	1108 (13)	0.812
Ankle oedema	119 (11)	977 (12)	0.482
Arrhythmia	136 (12)	879 (10)	0.054
Asthma/COPD	165 (15)	885 (11)	<0.001
Diabetes	205 (19)	1472 (18)	0.333
Gout	62 (6)	493 (6)	0.837
Heart failure	60 (5)	539 (6)	0.261
Hypercholesterolemia	252 (23)	1764 (21)	0.135
Myocardial infarction	66 (6)	606 (7)	0.168
Proteinuria/renal insufficiency	29 (3)	243 (3)	0.701
Stroke	98 (9)	692 (8)	0.416
Referral to an internist	359 (33)	2288 (27)	<0.001
Referral to a cardiologist	314 (29)	2031 (24)	0.002

COPD, chronic obstructive pulmonary disease.

Determinants influencing adoption of ARBs

Multivariable analyses showed that adoption of ARBs was associated with various determinants on physician level (Table 2, model 1). Adjusting for patient characteristics did not change the effects of physician level variables (Table 2, model 2). ARB prescribing was positively associated with frequent use of commercial information sources (OR = 2.0; 95% CI 1.5–2.6), but negatively associated with use of a computerized prescribing decision support system (OR = 0.8; 95%CI 0.7–1.0). GPs involved in providing pharmacotherapy education were less inclined to prescribe ARBs (OR = 0.7; 95%CI 0.5–0.9). Perceiving more benefits of ARBs in lowering blood pressure as compared to other antihypertensive drug classes was associated with higher adoption levels of ARBs. Finally, GPs who worked in single-handed practices or in rural areas were more likely to prescribe ARBs.

A number of factors appeared to be of little influence. No significant relation was observed between use of scientific medical journals, continuing education or other professional information sources and adoption of ARBs. GPs differed in the importance they assigned to specific drug characteristics, such as the importance of choosing a drug with high tolerability or low costs, but these

differences in values were not related to differences in higher or lower adoption levels for ARBs. Also, participation in trials was not a significant factor. Furthermore, ARB prescribing was not higher among GPs who perceived more influence or pressure of hospital physicians and patients to prescribe newer antihypertensive drugs. Patients who were referred to an internist or cardiologist, however, were more likely to be treated with ARBs.

Discussion

Twelve percent of the hypertensive patients were treated with ARBs in 2000, showing a clear adoption of ARBs in routine prescribing. Marketing of pharmaceutical industries was the main explanatory variable for variation in adoption between GPs. The efforts put into implementing clinical guidelines and practicing evidence-based medicine have not altered this influence. Many of the other potential determinants could not explain the observed variation, indicating that the adoption of ARBs was not driven by a preference for ARBs based on a rational decision process nor by professional or patient pressures. Further adjustment for influences of specialist-initiated prescribing and relevant patient characteristics did not change these findings.

Table 2

Association between physician and patient characteristics and the physician's choice to prescribe angiotensin II receptor blockers rather than other antihypertensive drug classes

	Adjusted odds ratios (95%CI) Model 1 ^a	Adjusted odds ratios (95%CI) Model 2	N (%)
<i>Variables related to physicians</i>			(n = 70)
Commercial information sources			
Never/seldom	1	1	30 (43)
Average	1.23 (0.98–1.55)	1.25 (1.00–1.58)	31 (44)
Often/always	1.93 (1.48–2.52)	1.96 (1.51–2.56)	9 (13)
Use of a prescribing decision support system			
No	1	1	36 (52)
Yes	0.80 (0.66–0.97)	0.80 (0.66–0.97)	33 (48)
Personal involvement in pharmacotherapy education			
No	1	1	50 (72)
Yes	0.67 (0.51–0.88)	0.70 (0.53–0.92)	19 (28)
Perceived benefits on blood pressure reduction (per mark higher for ARBs vs. other drug classes)	1.17 (1.04–1.32)	1.19 (1.05–1.34)	–
Practice type			
Partnership	1	1	44 (63)
Single-handed	1.35 (1.10–1.65)	1.37 (1.12–1.69)	26 (37)
Practice location			
Urban	1	1	36 (51)
Rural	1.67 (1.33–2.10)	1.76 (1.40–2.22)	34 (49)
<i>Variables related to patients</i>			(n = 9470)
Age (per year)		0.99 (0.98–0.99)	—
Asthma/COPD			
No		1	8420 (89)
Yes		1.51 (1.24–1.83)	1050 (11)
Myocardial Infarction			
No		1	8798 (93)
Yes		0.74 (0.55–1.00)	672 (7)
Referral to a cardiologist			
No		1	7125 (75)
Yes		1.41 (1.20–1.65)	2345 (25)
Referral to an internist			
No		1	6823 (72)
Yes		1.31 (1.13–1.51)	2647 (28)

^aMultilevel logistic regression model representing probabilities of prescribing ARBs as odds ratios, with 95% confidence intervals. Model 1: model with all significant physician level variables ($p < 0.05$). Model 2: model with all significant physician level variables adjusted for patient characteristics. An odds ratio > 1 means a higher adoption level of ARBs. CI, confidence interval.

The Netherlands take an intermediate position regarding the adoption of ARBs, since ARB use for hypertension ranged from less than 5% in the UK to 20% in Norway in 2000 (Fretheim & Oxman, 2005). It was hypothesized that the low adoption rate in the UK might be due to the efforts put into implementing evidence-based guidelines, whereas the high adoption rate in Norway might be the result of seeding trials (Fretheim & Oxman, 2005). Neither of these factors were the main driving forces for differences between adoption of ARBs within our country. We found that especially the use of commercial information sources was related with higher adoption levels of this new drug class.

Although many doctors acknowledge that the pharmaceutical industry tries to influence their prescribing, only few recognise themselves as being susceptible (Rutledge, Crookes, McKinstry, & Maxwell, 2003). Physicians who prescribed more ARBs did have a more positive perception of their effectiveness in lowering blood pressure. However, this is not an evidence-based judgment (Grobbee et al., 2001). Although we cannot determine a causal relationship, it is likely that promotional activities of the pharmaceutical industry played a role in the dissemination of these views. Pharmaceutical companies in The Netherlands devoted substantial resources to promote the advantages of ARBs in

terms of efficacy and tolerability (Bijl, 2000). Overall, the amount of money spent on ARB promotion in the year 2000 was 1.4 times higher than on all other classes of antihypertensives together (IMS Health, 2002b).

The finding that GPs using a computerized prescribing decision support system have not adopted ARBs at a high rate is promising, but should be seen in the light that such systems were only just becoming available on a large scale at the time of our study. This implies that they could not have played an important role in the adoption process of ARBs in the period up to the year 2000. It is therefore not clear whether the use of decision support systems leads to better prescribing or doctors who are better prescribers in the first place are more likely to use decision support systems. Prescribing decision support systems can provide evidence-based recommendations to clinicians during the electronic prescribing process. There is some evidence that this can lead to more rational and less costly prescribing in primary care (McMullin et al., 2004), but it has also become clear that these systems are used in variable frequency by GPs (Brenninkmeijer, 2005; Rogers, Jain, & Hayes, 1999). It is likely that especially GPs who already have a positive attitude towards evidence-based and cost-effective prescribing use these systems more frequently. This kind of attitude may also explain why personal involvement in providing pharmacotherapy education is associated with prescribing less ARBs. Cost-consciousness has been identified before as a relevant factor for restrictive prescribing of new drugs (Jacoby et al., 2003; Prosser & Walley, 2003).

Other studies showed that partnership practices adopted new drugs faster than single-handed practices, and suggested that continuous professional stimulation and other social factors might be a reason for this accelerated adoption (Steffensen et al., 1999; Williamson, 1975). We could not confirm this finding. On the contrary, adoption of new drugs was faster among physicians working in single-handed practices and in rural areas. This latter was also observed in a previous study (Tamblyn et al., 2003). Peer pressure was not found to be a driving force for the adoption of ARBs. There was, however, a clear effect of referrals to an internist or cardiologist on ARB treatment. Most GPs indicate that they usually continue prescriptions initiated by a hospital physician.

As an indicator for adoption we used prevalent prescribing of ARBs, since we aimed to identify

determinants for the adoption of ARBs for routine use in hypertension treatment. In previous studies, we observed that the rapid increase in ARB prescribing shortly after their introduction in the market was not limited to specific patient groups or initial prescribing (Greving et al., 2005; Greving et al., 2004). Dybdahl et al. (2004) demonstrated that most indicators of drug adoption correlate well with each other, except for the indicator that focuses on time until the first prescription of a new drug (Dybdahl et al., 2004). The latter is not surprising since there is a clear difference between the decision to prescribe a new drug for the first time ever and adopting a drug into routine prescribing.

An important strength of our study is that we were able to link GP, practice and patient characteristics to actual prescribing patterns of ARBs. The IPCI project gave us the advantage to achieve a high response rate to our questionnaire survey combined with the complete access to prescribing data of their hypertensive patient population. Consequently, there was a little chance of information and selection bias. Although the percentage of older, male GPs working in urban areas that participated in our survey was slightly higher compared to the entire population of Dutch GPs, the trends in choice of antihypertensive treatment in the period 1996–2000 correspond with general trends in antihypertensive prescriptions in the Netherlands (GIP, 2002; Greving et al., 2004; IMS Health, 2002a). The database provided patient specific information which enabled us to correct for the possible effect of specialist-initiated prescribing and patient characteristics. A limitation of the study was that our survey was conducted in 2003, when the first studies on hard endpoints of ARBs had become available. This may have changed the perception of GPs regarding this aspect. We do not expect, however, that major changes occurred regarding the use of information sources, professional network, and general physician characteristics.

In summary, the adoption rate of a new drug class is still determined more by the physicians' reliance on promotional information than by their use of professional information sources. Our findings underline the continuous need to implement effective ways of dealing with the influence of the pharmaceutical industry rather than relying on promoting evidence-based medicine through traditional professional channels.

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